PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Shoe cushioning, body mass and running biomechanics as risk factors for running injury: a study protocol for a randomised controlled trial
AUTHORS	Malisoux, Laurent; Delattre, Nicolas; Urhausen, Axel; Theisen, Daniel

VERSION 1 - REVIEW

REVIEWER	Dr. Sobhan Sobhani, PT, PhD Shiraz University of Medical Sciences, Shiraz, Iran
REVIEW RETURNED	07-May-2017

GENERAL COMMENTS	General comments: Thank you for giving me the opportunity to review this RCT protocol. In my opinion, by addressing the two important questions, this work will significantly contribute to our understanding of running biomechanics and running related injuries (RRIs). The protocol is well written and the study design seems sound. There is, however, one issue that deserves some attention. While the authors have considered various confounding factors in their study, one factor has been missed which is “the foot strike pattern”. Currently there is a great debate on-going on the association between different running foot strikes (e.g. forefoot strike vs. heel strike) as well as shoe cushioning with running injuries. It is believed that runners with different foot strike patterns are at risk of different RRIs. Thus I believe the lack of control for this factor might negatively influence the results. What do you think? Specific comments: Study population: L162-168: I believe you should be more specific about your selection criteria while defining “the leisure time (recreation) runner”. It is well know that intensity of running training a predictor factor for RRIs. Being able of running for 15 min and running at least once per week are not really good criteria. I myself used to run once per week for 5 km. I had a friend who would run 15 km and three times a week. We both considered ourselves as recreational runners regardless of the training intensity (frequency and running mileage). Please think about it. L180: allocation ratio 1:1? Are you sure about block size of 40?? Line 208: What do you mean by “more than one risk factor” and “clearance check”? Do you they will be excluded if they have one risk factor? What risk factors exactly? L213-214: Why do we need a random allocation here? They are supposed to run on a treadmill, aren`t they? L228-229: Since the body mass is one of the focus of your study,

	please be careful about the way you measure body mass at the baseline and the way the participants will measure their body mass later (e.g. being barefoot/shod or with heavy clothes) since even half kilogram difference might eventually count in your prediction model. L230: Will the Leg length be measured in weigh bearing (standing) or non-weigh bearing position (lying supine)? L241: Why do the participants need to report “the shoe pair used”. Aren`t they blind to the intervention? Aren`t they suppose to wear the same pair of shoes for the study period? L248-257: I strongly believe using two definitions for RRIs is confusing and somehow wrong. The second definition includes the lower back region in the definition while the first one not. One definition requires doctor consultation while the other not. The time-loss definition also differs. Have all these possible answers and injury criteria been considered in the TIPPS? Are you going to run two separate analyses based on the two different definitions? L260-261: “type of injury” and “description”: please elaborate what you mean by these questions and how a runner might define the type of injury him/herself. L280: What do mean by “HR”? Hazard Ratio perhaps? L 294: Aren`t shoe absorption properties pre-determined and different?? Why should you use an independent t-test to check whether they are different or not?!! Or am I missing something here? L 295-297: What are the within and between group factors in your two-way ANOVA model? ETHICS: Will the participants receive any incentives? Competing interests: What does LIH stands for? Could you provide more information about the nature of the external funding agencies? Are they shoe companies? I hope my comments help you improve your study protocol.

REVIEWER	Jean-Francois Esculier University of British Columbia, Canada
REVIEW RETURNED	20-May-2017

GENERAL COMMENTS	This manuscript describes the protocol for a randomized clinical trial comparing the effects of two different types of midsole hardness on running-related injuries. The same group of authors had published a similar study in the past, but the proposed study has a much bigger sample size, considers way more factors in analyses and uses footwear showing a greater difference in midsole hardness. I really believe that such study is needed, and I wish success to the authors on such project. I realize that this is a massive project involving an impressive number of variables; however, without getting the manuscript too heavy, I feel that additional details are needed on several points to facilitate reading. General comments Overall, I found the manuscript to be well written and relatively clear, but I feel that some improvements could be made with regards to the introduction and methods. When reaching the hypotheses, several variables were mentioned without being introduced earlier in the

	manuscript (stiffness, step length, step frequency, duty factor). I think the authors should briefly address them before reaching the end of the Introduction. As an example, they could reference Luedke et al. (MSSE, 2016) to support their hypothesis for step frequency and injuries. I also feel that details on outcomes are lacking. I understand that the main outcome will be the time to first injury. But there is no description of what will happen with these runners once they are injured. Is there a planned procedure for runners reporting pain or an injury? Will they be seen by a physician member of the research team? Will management of the injury be guided by some standardization? For example, if treatment is controlled for, will there be any possibility of gait retraining that could affect the outcomes? Or simply training loads modifications or exercises? If total number of injuries are also considered, how long after symptoms disappeared is a runner becoming "healthy again" and could potentially count as a new injury? As for biomechanical outcomes, I see a list of them in Table 1, but again, additional details are needed on data collection and analyses. Will there be any kinematics data collected? Please add sampling rate and filtering procedures for kinetics/kinematics data and how stance phase will be determined. How will you be calculating VLR? Duty cycle? Leg stiffness? Lastly, I was slightly confused by the retest session for some runners (final testing and testing in different shoes). Perhaps the authors should remove these sub-analyses from this study protocol. Specific comments Line 74: Reference 5, an Editorial by Leech et al., does not provide very strong arguments to support the statement that "long term consequences of (running overuse) injury include early-onset OA". Given the high prevalence of injuries in runners, yet no more risk for OA (Lo et al., 2016; Timmins et al., 2016; Alentorn-Geli et al., 2017), I believe the authors should modify their statement. Line 79: Considering adding the summary of 3 studies from Knapik et al. in JOSPT (2014) in references here. Line 113: "The role of shoe cushioning systems in RRI prevention remains unknown". I was expecting that the authors would be introducing a previous study from their group, published in BJSM in 2014. That study, referenced in the previous sentence (#28), suggested no differences in injury rates between two different midsole hardness. I suggest including a sentence to summarize findings from that study about here, and perhaps replace "unknown" by "unclear". (Such details at Line 122 should be included before). Line 129: I suggest introducing the word stiffness in the Introduction before Hypothesis 1. Line 133: Why peak VGRF and not vertical loading rate? In the studies cited in the introduction, VLR is way more relevant than peak VGRF. Line 165: The presence of a current RRI is an exclusion criterion, but no details are provided on this important point. What is your

	definition of a “current” RRI? Since how much time should potential participants be pain free before enrolling? Line 185: How is shoe size determined? This could have implications for foot pain/injuries related to inadequate fitting. Line 214: As I understand it, runners will be trying their new shoes for the first time while in the lab for testing. I really like the idea of testing runners in their assigned shoes. Do you think it would be appropriate to leave them one or two trial runs on their own before conducting biomechanical testing? If not, is it possible that runners may change their mechanics to adapt to the shoes after a few running sessions, just like you are trying to control for by reassessing those running at 10km/h? Line 231: Could the authors comment on the measurement error for their “direct” measurement of leg length? Line 274: Is there a maximum running volume as part of the exclusion criteria? What did the investigators plan in the event that some runners wear out their assigned shoes during the 6-month period? Will they be getting new ones with similar features? Line 284: This paragraph is not that clear to me. Are those people the same as those who will be reassessed at the end of the 6-month period? If not, it would be relevant to add precisions on these sub-analyses (the final testing session). Line 302: About the right-censored runners: I think the authors should report exact reasons for such classification when they report results (not just mentioning that they were right-censored). A statement saying “Reasons for drop-outs and right censoring will be reported” is recommended.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Sobhan Sobhani, PT, PhD
Shiraz University of Medical Sciences, Shiraz, Iran
Please state any competing interests or state ‘None declared’: None declared
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Thank you for giving me the opportunity to review this RCT protocol. In my opinion, by addressing the two important questions, this work will significantly contribute to our understanding of running biomechanics and running related injuries (RRIs). The protocol is well written and the study design seems sound. There is, however, one issue that deserves some attention. While the authors have considered various confounding factors in their study, one factor has been missed which is “the foot strike pattern”. Currently there is a great debate on-going on the association between different running foot strikes (e.g. forefoot strike vs. heel strike) as well as shoe cushioning with running injuries. It is believed that runners with different foot strike patterns are at risk of different RRIs. Thus I believe the lack of control for this factor might negatively influence the results. What do you think?
Dear Dr. Sobhan Sobhani,
We would like to thank you for your feedback and your constructive comments. We sincerely believe that they allowed us to improve the quality of the present paper. We hope that our corrections and clarifications are satisfactory.
Please find below a point-by-point reply to your general and specific comments.

We agree with you on the fact that “It is believed that runners with different foot strike patterns are at risk of different RRIs”. However, this is common belief. There is no evidence of such association in the scientific literature. By the way, the definition of foot strike (rear-, mid-, or forefoot strike) is unclear and has been used in an overly simplistic way. Also, the strike pattern can be investigated via some proxy variables such Peak Vertical Ground Reaction Force or Peak Vertical Loading Rate, which will be measured in our study. Finally, it is extremely challenging to add kinematics analyses (with 2D or 3D analysis) to measure the foot-ground angle in the present study that aims to recruit 800 runners.

Specific comments:
Study population: L162-168:
I believe you should be more specific about your selection criteria while defining “the leisure time (recreation) runner”. It is well know that intensity of running training a predictor factor for RRIs. Being able of running for 15 min and running at least once per week are not really good criteria. I myself used to run once per week for 5 km. I had a friend who would run 15 km and three times a week. We both considered ourselves as recreational runners regardless of the training intensity (frequency and running mileage). Please think about it.
We thank you for your comment. We have already carefully considered the targeted population for the present study. Here are the arguments for including leisure-time (recreational) runners without too many restrictions: 1) given the study design and the sample size, we can reasonably assume that the 2 study groups will be well balanced regarding the profile of the participants (e.g. running level or experience), 2) the more specific the population, the lower the external validity, 3) the 2 runners that you described correspond to the extreme and opposite profiles of the population of recreational runners. We do not want to exclude any of these 2 categories. However, since we record information related to the runners’ training pattern prior to the study, we will be able to investigate if there is an interaction between runner profile and shoe cushioning on injury risk.

L180: allocation ratio 1:1? Are you sure about block size of 40??
Yes, the 2 study groups will be equally distributed regarding the sample size (1:1 ratio), and the randomisation list guarantee this balance every 40 subjects. This means that the theoretical maximal difference between groups will be 20. Please, note that an imbalance in the number of participants recruited in each group would not induce a bias (i.e., if we cannot complete the last block at the end of the recruitment).

Line 208: What do you mean by “more than one risk factor” and “clearance check”? Do you they will be excluded if they have one risk factor? What risk factors exactly?
Thank you for pointing this out. We have clarified the sentence to specify that the questionnaire aims at detecting cardiovascular risk factors. The new sentence is: “Every participant responding positively to any of the symptom-based questions or presenting more than one cardiovascular risk factor will be invited for a clearance check by a sports medical doctor prior to the test.” The questionnaire has been added as supplementary online material. The participants with only one risk factor will not be excluded as the list of factors include age over 45 years, smoking or high blood pressure. We could not exclude a participant on the basis of one single risk factor (again, this would be a bias for external validation), but those with more than one factor will need the clearance from a medical doctor.

L213-214: Why do we need a random allocation here? They are supposed to run on a treadmill, aren`t they?
We refer to the randomised allocation of the participants to the study groups. The participants will be tested on the treadmill with the study shoes that they will just have received. The sentence has been reedited and is now “The biomechanical running analysis will be performed on an instrumented treadmill (M-Gait, Motekforce Link Amsterdam, The Netherlands) in the randomly allocated study shoes.”

L228-229: Since the body mass is one of the focus of your study, please be careful about the way you measure body mass at the baseline and the way the participants will measure their body mass later (e.g. being barefoot/shod or with heavy clothes) since even half kilogram difference might eventually count in your prediction model.
Thank you for pointing this out. We omitted to report that body height will also be measured at baseline. The new sentence is: “The body mass and height of each participant will be measured barefoot and in running clothes before the treadmill running test”. As described page 10 line 226-235, body mass and body composition measurements will be obtained with the Tanita SC-240 MA model.

L230: Will the Leg length be measured in weigh bearing (standing) or non-weigh bearing position (lying supine)?
Thanks again for your comment. We have added this information in the text. The measure between the anterior superior iliac spine and the medial malleolus is perform with the participant in a supine position, while the distance between the greater trochanter and the ground will be measured in a standing position.

L241: Why do the participants need to report “the shoe pair used”. Aren`t they blind to the intervention? Aren`t they suppose to wear the same pair of shoes for the study period?
The participants will be blinded to the intervention. Also, they will be required to use the study shoes for all their running sessions during the 6-month follow-up period. However, some of them might need exceptionally to use another pair of running shoes for one of their sessions (forgot the shoes at home, shoes are soaked because of the last session in the rain…). We will ask the participants to report the shoes used for each of the running sessions. Their study shoes will already be available in the system and identified with an anonymous shoe ID. We will use the data collected on TIPPS to measure the adherence to the study intervention.

L248-257: I strongly believe using two definitions for RRIs is confusing and somehow wrong. The second definition includes the lower back region in the definition while the first one not. One definition requires doctor consultation while the other not. The time-loss definition also differs. Have all these possible answers and injury criteria been considered in the TIPPS? Are you going to run two separate analyses based on the two different definitions?
The participants only have to report any painful episode that forced them to adapt or interrupt their training accordingly. The research team will subsequently check if the event reported on TIPPS can be defined as a RRI according to each of the definition. We have clarified this on page 11 lines 253-255 as well as on page 12 lines 270-272. Two separate analyses will be performed to investigate if our former definition (used in our previous papers) and the new definition (consensus) give similar results (sensitivity analysis).
By the way, none of the definitions require physician consultation, although the consensus definition does include the pains that require the runner to consult a physician or another health professional.

L260-261: “type of injury” and “description”: please elaborate what you mean by these questions and how a runner might define the type of injury him/herself.
Our injury form is based on the OSICS classification system for sports injuries. The type of injury is a rather general question and aims to distinguish between fracture, tendon injury, abrasion, sprain, muscle tears… Description of the injury refers to a free text field that allows the participants to provide the research team with any additional information regarding the injury (how it happened and developed, treatment…). The latter has been added in the text.

L280: What do mean by “HR”? Hazard Ratio perhaps?
You are right. Hazard rate ratio had not been defined above in the manuscript. HR is now defined in the sample size section.

L 294: Aren`t shoe absorption properties pre-determined and different?? Why should you use an independent t-test to check whether they are different or not?!! Or am I missing something here?
The mechanical properties of the shoe versions are predefined and have been measured in a few prototypes produced during the preparation phase of the study. We noticed that there could be some variability in the mechanical properties of the study shoes. Therefore, the shoe manufacturer will also assess the mechanical properties of a subset of the shoes that will be produced for the study in order to quantify accurately the difference between the 2 shoe models.

L 295-297: What are the within and between group factors in your two-way ANOVA model?
As suggested by reviewer n°2, this sub-analysis was removed from the present manuscript (please, see our comment below).

ETHICS:
Will the participants receive any incentives?
The participants will not receive any incentive. They will receive the pair of running shoe for free, as well as a feedback on the running test performed on the instrumented treadmill at baseline (after completion of the study).

Competing interests:
What does LIH stands for? Could you provide more information about the nature of the external funding agencies? Are they shoe companies?
LIH stands for Luxembourg Institute of Health. It has been defined in the new version of the manuscript. The shoes will be provided by a sport equipment manufacturer, who is not involved in the data collection and analysis of the results. The study is co-funded by the 2 parties.

I hope my comments help you improve your study protocol.
Regards,
Dr. Sobhan Sobhani, PT, PhD

Reviewer: 2
Jean-Francois Esculier
University of British Columbia, Canada
Please state any competing interests or state ‘None declared’: None declared
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This manuscript describes the protocol for a randomized clinical trial comparing the effects of two different types of midsole hardness on running-related injuries. The same group of authors had published a similar study in the past, but the proposed study has a much bigger sample size, considers way more factors in analyses and uses footwear showing a greater difference in midsole hardness. I really believe that such study is needed, and I wish success to the authors on such project. I realize that this is a massive project involving an impressive number of variables; however, without getting the manuscript too heavy, I feel that additional details are needed on several points to facilitate reading.
Dear Dr. Jean-François Esculier,
We would like to thank you for your extensive and constructive criticisms on our manuscript. We are convinced that your input has helped us to improve significantly our paper, and we hope that our corrections and clarifications are satisfactory.
Please find below a point-by-point reply to your general and specific comments.

General comments

Overall, I found the manuscript to be well written and relatively clear, but I feel that some improvements could be made with regards to the introduction and methods. When reaching the hypotheses, several variables were mentioned without being introduced earlier in the manuscript (stiffness, step length, step frequency, duty factor). I think the authors should briefly address them before reaching the end of the Introduction. As an example, they could reference Luedke et al. (MSSE, 2016) to support their hypothesis for step frequency and injuries.
Since the intervention of the present study is shoe cushioning, we developed the introduction on the basis of the current knowledge related to the effect of shoe cushioning on running biomechanics (i.e. mainly VGRF and VLR) as well as on injury risk. Since other variables will be explored, we have also briefly introduced some of them according to your suggestion.

I also feel that details on outcomes are lacking. I understand that the main outcome will be the time to first injury. But there is no description of what will happen with these runners once they are injured. Is there a planned procedure for runners reporting pain or an injury? Will they be seen by a physician member of the research team? Will management of the injury be guided by some standardization? For example, if treatment is controlled for, will there be any possibility of gait retraining that could affect the outcomes? Or simply training loads modifications or exercises? If total number of injuries are also considered, how long after symptoms disappeared is a runner becoming "healthy again" and could potentially count as a new injury?
The procedure to report pains and injuries, as well as the validation of the data self-reported by the participants are already described in the manuscript page 11 and 12 (data on outcome and follow-up). No research question is related to the type of injury or injury management such as gait retraining, treatment, or training load adjustment. As the main outcome is the first injury, this study focuses on primary prevention. Recurrent injuries will not be included in the analyses. We acknowledge that high quality research is needed on the management of RRI, but this is not the purpose of the present project.

As for biomechanical outcomes, I see a list of them in Table 1, but again, additional details are needed on data collection and analyses. Will there be any kinematics data collected? Please add sampling rate and filtering procedures for kinetics/kinematics data and how stance phase will be determined. How will you be calculating VLR? Duty cycle? Leg stiffness?
No kinematics data collection will be performed in the present study. We could not add this aspect to our protocol given the targeted sample size. The sampling rate for the kinetics recordings has been added to the manuscript. However, the filtering procedures as well as the data processing method for the determination of the stance phase and the calculation of VLR and leg stiffness will have to be presented in the methods section of the future paper presenting the original results. Indeed, we might need to fine-tune some parameters based on the quality of our recordings. Therefore, we prefer not to provide this kind of details in the present manuscript.

Lastly, I was slightly confused by the retest session for some runners (final testing and testing in different shoes). Perhaps the authors should remove these sub-analyses from this study protocol.
A within-subject analysis is much more robust to demonstrate and quantify the difference between 2 shoe conditions. This part of the study is totally independent of the RCT, and the 2 dataset will not be merged. For the sake of clarity, we have decided to remove this part of the project from the present manuscript, which focuses on the RCT. Figure 1 (Flow chart) was adapted accordingly.

Specific comments
Line 74: Reference 5, an Editorial by Leech et al., does not provide very strong arguments to support the statement that "long term consequences of (running overuse) injury include early-onset OA". Given the high prevalence of injuries in runners, yet no more risk for OA (Lo et al., 2016; Timmins et al., 2016; Alentorn-Geli et al., 2017), I believe the authors should modify their statement.

Thank you for pointing this out. We recognise that the association between RRI and future development of OA is weak and that it could be confounded by other risk factors. Thus, we played down our statement and replaced the reference by the latest systematic review on the topic (Alentorn-Geli et al., 2017).

Line 79: Considering adding the summary of 3 studies from Knapik et al. in JOSPT (2014) in references here.
Thank you for your suggestion. We have added the reference.

Line 113: “The role of shoe cushioning systems in RRI prevention remains unknown”. I was expecting that the authors would be introducing a previous study from their group, published in BJSM in 2014. That study, referenced in the previous sentence (#28), suggested no differences in injury rates between two different midsole hardness. I suggest including a sentence to summarize findings from that study about here, and perhaps replace “unknown” by “unclear”. (Such details at Line 122 should be included before).
We agree that it is worth presenting more information about our previous study on midsole hardness. A sentence summarising the findings was added, and we replaced “unknown” with “unclear” as suggested.

Line 129: I suggest introducing the word stiffness in the Introduction before Hypothesis 1.
Thank you for your comment. We have explained in the introduction that shoe cushioning will be characterised by the stiffness at the heel and quantified by standardised impact test (page 6, line 129-130).

Line 133: Why peak VGRF and not vertical loading rate? In the studies cited in the introduction, VLR is way more relevant than peak VGRF.
We totally agree with you. We have reedited the hypotheses 4, 5 and 6.

Line 165: The presence of a current RRI is an exclusion criterion, but no details are provided on this important point. What is your definition of a “current” RRI? Since how much time should potential participants be pain free before enrolling?
The participants should not have suffered any major problem in the previous 12 months, nor any running impeding injury over the previous month. This has been clarified in the manuscript and is now: “Volunteers will be excluded in case of any contraindication to perform running activity, prior (<12 months) surgery or major trauma to the lower limbs or lower back region, any running impeding injury over the previous months, or use of orthopaedic insoles for running activities.”

Line 185: How is shoe size determined? This could have implications for foot pain/injuries related to inadequate fitting.
The participants will have the opportunity to try out the shoes and choose the size that fits best to their feet during their visit to the laboratory. Blisters does not fit with our definition for RRI (musculoskeletal pain…).

Line 214: As I understand it, runners will be trying their new shoes for the first time while in the lab for testing. I really like the idea of testing runners in their assigned shoes. Do you think it would be appropriate to leave them one or two trial runs on their own before conducting biomechanical testing? If not, is it possible that runners may change their mechanics to adapt to the shoes after a few running sessions, just like you are trying to control for by reassessing those running at 10km/h?
Actually, we need data at baseline for several reasons. The main one is that some runners might sustain an injury during the first sessions. If the injury occurs before the test, these participants would be lost for the study, while they got an injury. So it would introduce a huge bias in the analyses. We understand your point here, and we totally agree with you. The ideal protocol would be to test the

participants at different time points during the follow-up, and include the biomechanical variables as time-dependant covariant in our adjusted Cox regression analysis. We have already applied this statistical approach. This is not the issue. We are sure that you understand that it would be extremely challenging to repeat the running test several times with 800 participants.
Also, some studies showed that most of the adaptations occur during the first 8 minutes when changing shoe type (Delattre et al. 2013). This is the adaptation period we have foreseen before the first recording.

Line 231: Could the authors comment on the measurement error for their "direct" measurement of leg length?
A reference is provided regarding the "direct" measurement of leg length as well as its accuracy. Unfortunately, little useful information is available on the accuracy. Only ICC were provided. Inter-rater reliability seems to be good (ICC: 0.99) but the concordance between the "direct" method and radiographic measurement is lower (ICC: 0.80). We strongly believe that this information is not worth being presented in the paper.

Line 274: Is there a maximum running volume as part of the exclusion criteria? What did the investigators plan in the event that some runners wear out their assigned shoes during the 6-month period? Will they be getting new ones with similar features?
We have no argument to exclude a participant due to excessive running volume (what would excessive mean). On the contrary, this could introduce sampling bias. If a participant experiences abnormal use and wear with their shoes, the latter will be replaced in the limit of their availability. If a participant covers a large distance and wears out the shoes before the end of the 6-month period, the participant will be right-censured. This will not bias the analysis (see Nielsen et al., 2016), and the participant will have largely contributed to the study given the total distance covered.

Line 284: This paragraph is not that clear to me. Are those people the same as those who will be reassessed at the end of the 6-month period? If not, it would be relevant to add precisions on these sub-analyses (the final testing session).
This section referred to the within-subject analysis that aimed to show the effect of shoe condition on running biomechanics. As explained above, that part has been removed from the present manuscript.

Line 302: About the right-censored runners: I think the authors should report exact reasons for such classification when they report results (not just mentioning that they were right-censored). A statement saying "Reasons for drop-outs and right censoring will be reported" is recommended.
Thank you for your comment. The report of the reasons for drop-out is common practice in prospective studies and was indeed foreseen. We have also added a statement regarding the report of the right-censoring as suggested.

VERSION 2 – REVIEW

REVIEWER	Dr. Sobhan sobhani Shiraz University of Medical Sciences, Shiraz, Iran
REVIEW RETURNED	05-Jun-2017

GENERAL COMMENTS	Thank you for your complete responses. I believe the protocol has been improved significantly. With regard to strike type, of course it is up to you but I still suggests that you identify at least heel strikers vs. none heel strikers using the GRF data. This could help us to understand as the whether a specific strike type could be of importance in developing running injuries or not. I wish you all the

	best with this valuable project.

REVIEWER	Jean-Francois Esculier University of British Columbia Canada
REVIEW RETURNED	26-Jun-2017

GENERAL COMMENTS	I would like to thank the authors for their detailed response to my previous comments and to comments from the other Reviewer. Overall, I feel that most of them have been addressed. Obviously, this manuscript being a study protocol (already funded and registered), changes to the study itself are limited. I understand that. However, I think some precisions still need to be added to clarify what will be done (not to change the protocol but to facilitate understanding). You mention that the primary outcome is “first-time injury”. This expression is still unclear to me: are you considering the time to first injury or the total number of new injuries that happened over the course of the study period (or both)? Good on providing the definitions and how you will analyze injuries using the 2 different definitions, but the actual outcomes need a little more details I think. Line 172: Your response mentions that runners with an injury on the previous month will be excluded; yet, your sentence says “previous months”. If it is only one month, remove the “s” here. I forgot to mention it in my first round of comments, but is there a consideration of previous footwear (e.g. minimalist) in exclusion criteria or as a confounding factor to control for in analyses? Basically, are you just including runners who are used to run with traditional cushioned shoes? Transition injuries may occur when switching footwear category. Line 198: Will footwear be integrated gradually or with some sort of transition for runners who already run higher volume (e.g. 60+ km/week)? This is the reason why I asked if there were any exclusion criteria relative to running volume. Switching footwear all of a sudden could lead to injuries. In such cases, these would classify as transition injuries and not injuries related to the type of footwear that is being evaluated in your study.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Dr. Sobhan sobhani
Shiraz University of Medical Sciences, Shiraz, Iran Please state any competing interests or state ‘None declared’: None declared
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Dear authors,
Thank you for your complete responses. I believe the protocol has been improved significantly. With regard to strike type, of course it is up to you but I still suggests that you identify at least heel strikers vs. none heel strikers using the GRF data. This could help us to understand as the whether a specific strike type could be of importance in developing running injuries or not. I wish you all the best with this

valuable project.

Regards,
Dr. Sobhan Sobhani, PT, PhD

Dear Dr Sobhani,
Thank you for your feedback and comments. As explained in our previous response, we will unfortunately not be able to determine the part of the foot that touches the ground first, or the foot-ground angle at touch down. Nevertheless, as you suggested, we will consider classifying the participants depending on the presence or absence of a transient impact peak, and investigate the association with the development of running injury.

Reviewer: 2
Jean-Francois Esculier
University of British Columbia, Canada
Please state any competing interests or state 'None declared': None
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I would like to thank the authors for their detailed response to my previous comments and to comments from the other Reviewer. Overall, I feel that most of them have been addressed. Obviously, this manuscript being a study protocol (already funded and registered), changes to the study itself are limited. I understand that. However, I think some precisions still need to be added to clarify what will be done (not to change the protocol but to facilitate understanding).

Dear Dr Esculier,
Thank you for your feedback and constructive comments. We hope that our clarifications are satisfactory. Please find below a point-by-point reply to your comments.

You mention that the primary outcome is "first-time injury". This expression is still unclear to me: are you considering the time to first injury or the total number of new injuries that happened over the course of the study period (or both)? Good on providing the definitions and how you will analyze injuries using the 2 different definitions, but the actual outcomes need a little more details I think. Survival analyses, or time-to-event analyses, concern analysing the time to occurrence of an event of interest, in this case running injury. We have clarified the sentence on line 247, which is now: "The primary outcome is the first RRI occurring during the follow-up."

Line 172: Your response mentions that runners with an injury on the previous month will be excluded; yet, your sentence says "previous months". If it is only one month, remove the "s" here.
Thank you for pointing this out. We have corrected the typo.

I forgot to mention it in my first round of comments, but is there a consideration of previous footwear (e.g. minimalist) in exclusion criteria or as a confounding factor to control for in analyses? Basically, are you just including runners who are used to run with traditional cushioned shoes? Transition injuries may occur when switching footwear category.
In one of our previous studies, we asked the participants to bring their current running shoes in order to characterise them. The aim was to classify the participants according to the drop of the shoes they were used to before the study. However, we realised that this is simply impossible for most of the participants because: 1) some runners were running in different pairs of running shoes alternatively, 2) some had changed their running shoes recently, 3) some had not practiced running for several months, 4) some had used minimalist shoes occasionally, 5) some used to run with minimalist shoes but took up conventional cushioned shoes… In conclusion, a meaningful and reliable classification of

runners according to their prior shoe use turned out to be impossible.
Secondly, given the large sample size and the design (random allocation), if transition injuries occurred because of switching footwear category, it will most likely equally impact the two study groups.

Line 198: Will footwear be integrated gradually or with some sort of transition for runners who already run higher volume (e.g. 60+ km/week)? This is the reason why I asked if there were any exclusion criteria relative to running volume. Switching footwear all of a sudden could lead to injuries. In such cases, these would classify as transition injuries and not injuries related to the type of footwear that is being evaluated in your study.
In our previous studies, we observed that most runners regularly used conventional shoes (or shoes with a drop > 8mm). Also, the shoe cushioning of the prototypes will remain within the range of the models available on the market. So we think that the transition will be less critical for this study, for example when comparing with a protocol that requires switching from conventional shoe to minimalist shoes. By the way, we do not think that those running mainly with minimalist shoes will wish to participate in our study on cushioning.